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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,026	07/06/2001	Andre Stamm	107664.115US3	7379

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,026	STAMM ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *162-239* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *162-239* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Information Disclosure Statements (IDS) filed 06/25/04, 06/16/04, & 03/30/04 and the Amendment to the Specification and Claims, Applicant's Arguments/Remarks and the Terminal Disclaimer, all filed 03/30/04 is acknowledged.

Upon further consideration, the previous Non-Final Office Action filed 12/20/03 has been *withdrawn*. The following are the new grounds for rejection:

Claims 162-239 are pending. New claim 239 has been added. Claims 162-239 are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 162-239 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mughal *et al.* (US Pat. No. 4,524,060) in view of Boyer (US Pat. No. 4,800,079) and further in view of Kerc *et al.* (US Pat. No. 6,042,847) or Klimesch *et al.* (US Pat. No. 5,073,379).

Mughal *et al.* teach a pharmaceutical composition comprising an inert core of non-pareil seeds, whereby the inert core is coated with a mixture of hydrophilic polymer and micronized drug (indoramin) (see reference column 2, lines 19-43) and Examples.

In a preferred dosage form, the composition of the invention is prepared by applying the ingredients, with adhesive, to an inert core, which acts as a physical support, e.g., non-pareil seeds; and then providing a sustained release or enteric coating, preferably in the form of a film applied to the pellet (col. 2, lines 19-24).

In another embodiment, the pharmaceutical composition is in capsule form comprising sustained release pellets each containing about 50-95% by weight of a mixture of micronized drug (indoramin) or a pharmaceutically acceptable salt thereof, with up to about 25% of a hydrophilic polymer, up to about 10% by weight of a wetting agent (surfactant) and about 1-10% of a disintegrant (modified starch, cross-linked PVP) the mixture being in the form of a non-compressed pellet (col. 2, lines 4-35).

The ratio of drug (indoramin) to the hydrophilic polymer is taught to be about 30:1 to about 2:1 (col. 2, lines 38-40). The drug (indoramin) is micronized to a particle size in which 90% or particles are less than or equal to 15 μ (col. 2, lines 37-38). The inert core is a non-pareil seed of from about 500 to 840 μ diameter (claim 10).

Mughal et al. teach the presence of polymers, as well as mixtures of polymers, that include, for example, polyvinylpyrrolidone, ethyl cellulose, polyethylene glycol, hydroxypropyl cellulose, methylcellulose, hydroxypropylmethyl cellulose and polyacrylate resins such as Eudragit (col. 3, lines 6-19).

A process for preparing the pharmaceutical composition is also taught which comprises intimately mixing micronized drug (indoramin) with polymers, water-channeling agents, wetting agents and excipients, such as lactose (col. 3, lines 50-59).

The degree of micronization and the ratios of micronized drug (indoramin), water-channeling agent (hydrophilic polymer), wetting agent and disintegrant are adjustable so that at least about 80% dissolution of drug occurs in gastrointestinal media within about 24 hours (col. 2, lines 41-49).

The Examples demonstrate various embodiments of the invention for preparing coated or uncoated pellets on non-pareil (inert) seed cores. Example 1, for instance, demonstrates the preparation of indoramin hydrochloride sustained release pellets, wherein non-pareil seeds (e.g., 840-500 μ) are wetted evenly by spraying on a ca. 5% adhesive solution of polyvinylpyrrolidone (PVP) in isopropyl alcohol adhesive (IPA) (col. 4-7).

Regarding the instant weight ratios and dissolution release rates, it is the position of the Examiner that there is no criticality observed in the ratios or dissolution rates, since one of ordinary skill in this art would be capable of determining suitable weight ratios or dissolution rates through the use of routine or manipulative experimentation to obtain the best possible results, as these are variable parameters. Moreover, the prior art teaches a similar formulation whereby the inert cores are coated with a mixture of drug and

hydrophilic polymer and also teaches similar weight ratios and dissolution rates whereby the properties imparted by the ratios/rates would also allow for a similar effect.

Mughal *et al.*, while teaching a pharmaceutical composition comprising inert core particles coated with an admixture of drug and hydrophilic polymer, are lacking in the sense that they do not teach the particular drug, fenofibrate.

Boyer ('079) teaches a granular medicine based on fenofibrate, whereby each granule comprises an inert core constituted with hydrosoluble carrier particles, a layer based on fenofibrate and a protective layer. In the layer based on fenofibrate, the fenofibrate is present in the form of crystalline microparticles of dimensions not greater than 30 microns (see reference column 2, lines 10-17) & Abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the combined teachings of Boyer within Mughal *et al.* to obtain inert core particles or non-pareil seeds coated with any active ingredient, particularly fenofibrate, because Boyer teaches such a granular medicine, that is based on fenofibrate to effectively treat conditions of hyperlipidemia, hypercholesterolemia and hypertriglyceridemia, whereby the core is inert and the fenofibrate is provided in a separate layer, to allow for more uniform absorption of the active ingredient and similarly, Mughal et al. teach a pharmaceutical composition comprising inert cores or non-pareil seeds coated with an admixture of drug and polymer, wherein the drug is contained outside the core. The expected result would be an effective fenofibrate composition with improved solubility for the treatment of hyperlipidemia and related disease conditions.

Mughal *et al.* do not teach the pharmaceutical composition in *tablet* dosage form.

It is obvious to one of ordinary skill in this art to formulate pharmaceutical compositions in an array of forms that include capsules, tablets, granules, pellets and the like. Such skill is also evident from the reference of Kerc *et al.* ('847) or Klimesch *et al.* ('379).

Kerc *et al.* ('847) teach a three-phase fenofibrate pharmaceutical formulation for daily peroral application, wherein the composition can be in the form of *tablets or capsules* (see reference column 1, lines 18-22).

Klimesch *et al.* ('379) teach a fenofibrate preparation comprising a mixture of one or more pharmaceutical active compounds with hydrophilic polymers, wherein the composition can be produced in the form of *tablets* or alternatively very small tablets which are advantageously filled into *capsules*, instead of conventional granules (see reference column 3, lines 1-18); (col. 3, line 67 – col. 4, line 56); (col. 5, line 10) and Abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Kerc *et al.* or alternatively, Klimesch *et al.* within the teachings of Mughal *et al.* because Kerc *et al.* and Klimesch *et al.* explicitly teach that the fenofibrate composition that can be either in the form of tablets or capsules and similarly Mughal *et al.* teach a drug formulation in the form of capsules. The expected result would be a tabletted or capsular pharmaceutical composition, as similarly desired by Applicant.

Prior Art made of record, not relied upon, and deemed relevant by the Examiner:

US Pat. No. 4,684,516	Bhutani	08/1987
US Pat. No. 2,953,497	Press	09/1960

Response to Arguments

Applicant's arguments with respect to claims 162-238 have been considered but are moot in view of the new ground(s) of rejection.

Claims 162-239 have now been rejected under §35 USC 103(a) over Mughal *et al.* (US '060) in view of Boyer (US '079) and further in view of Kerc *et al.* (US '847) or Klimesch *et al.* (US '379).

The prior art teaches and suggests pharmaceutical formulations comprising inert core particles, wherein the particles are coated with an admixture of active ingredient and hydrophilic polymer. Active ingredients taught are fenofibrate to effectively treat hyperlipidemia, hypercholesterolemia and hypertriglyceridemia. The prior art teaches such formulations in tablet, capsule, granular and pellet dosage formulations and teaches suitable weight ratios and dissolution profiles. Since the prior art teaches the same ingredients applied for the same intended purpose and for the same field of endeavor as that desired by Applicant, the instant invention is rendered *prima facie* obvious over the cited prior art of record.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays from 8:00 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

H. N. Sheikh H.N.S.

Patent Examiner

Art Unit 1615

August 18, 2004

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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